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10/533,700	10/28/2005	Toshiyuki Takai	4439-4032	6164

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MORGAN & FINNEGAN, L.L.P.
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101

EXAMINER	
SINGH, ANOOP KUMAR	

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1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/533,700	TAKAI ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment to the specification and claims filed on March 5, 2007, has been received and entered. Claims 1-3, 6-9 have been amended, while claims 4-5 have been canceled. Claims 6-8 that were objected and withdrawn in previous office action are rejoined in view of amendments to the claims. Applicants have also added claim 9.

Withdrawn-Claim Objections

Claims 6-8 objected to under 37 CFR 1.75(c) as being in improper form is withdrawn in view of amendments to the claims. It is noted that Examiner had withdrawn claims 6-8 as they were dependent on a multiple dependent claim. See MPEP § 608.01(n). It is noted that, examiner inadvertently included claims 6-8 in the statements of 35 U.S.C. 112, second paragraph rejection. However, the inclusions of these claims were not required as the rejection was only intended for claims 1-3. This is further evidenced by recitation of "claims 6-8 are not further treated on the merit "see MPEP § 608.01(n) in the beginning of the office action in claim objection section (see page 2 of the office action, line 12-13) and rest of rejections.

Claims 1-3, 6-9 are under consideration.

New-Claim Rejections-Necessitated by amendments - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) a mouse showing symptoms of peripheral

neuropathy leading to paralysis of its tail and hind leg and elevated levels of antibody titer against GQ1b, wherein the I mouse is obtained by immunizing with gangliosides GQ1b a homozygous transgenic mouse whose genome comprises a disruption of the exon encoding S2 and EC1 of the FCγRIIB wherein said transgenic mouse does not produce Fc.gamma.RIIB protein, and

(ii) a method for screening a test agent for improving symptoms of peripheral neuropathy leading to paralysis of the tail and hind leg, comprising the steps of: a) administering a test agent to mouse showing the symptoms of peripheral neuropathy leading to paralysis of its tail and hind leg wherein said mouse is obtained by immunizing with GQ1b a homozygous transgenic mouse whose genome comprises a disruption of the exon encoding S2 and EC1 of the FCγRIIB wherein said transgenic mouse does not produce Fc.gamma.RIIB protein, b) determining or assessing at least one symptom selected from the group consisting of peripheral neuropathy leading to paralysis of its tail and hind leg and GQ1b antibody level in both mouse and, c) comparing the results with a mouse that is used as control to which the test substance is not administered, wherein a decrease in the severity of at least one said symptom in the first mouse to which the test substance is administered compared to the second mouse to which the test substance is not administered indicates that the test substance is effective to improve said symptom,

does not reasonably provide enablement for model of Guillain-Barre syndrome (GBS) or Fisher syndrome or deficiency of the FCγRIIB gene or any other "mouse" showing phenotype as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ

1400, 2d at 1404. Such factors are: (1) The breadth of the claims; (2) The nature of the invention; (3) The state of the art; (4) The level of one of ordinary skill in the art; (5) The level of predictability in the art; (6) The amount of direction and guidance provided by Applicant; (7) The existence of working examples; and (8) The quantity of experimentation needed to make and/or use the invention.

The office has analyzed the specification in direct accordance to the factors outlines in *In re Wands*. MPEP 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on factors discussed in MPEP 2164.01(a) and the evidence as whole, it is not necessary to discuss each factor in written enablement rejection." These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform "undue experimentation" to make and/or use the invention and therefore, applicant's claims are not enabled.

Claims 1-3, 6-8 and 9 are broad in scope. The following paragraph will outline the full scope of the claims. Claimed invention recites a mouse model of GBS that can be obtained by immunizing an homozygous FCgRIIB gene deficient mouse with gangliosides GQ1b. Claim 2 is directed to a mouse model of GBS that is Fisher syndrome encompassing any mouse showing phenotype consistent with GBS or Fisher syndrome. Claim 3 limits the mouse model of claims 1 and 2 to include GBS that develops in peripheral and paralysis of its tail and hind legs and shows elevated antibody titer. Claims 6-8 are directed to a screening method of a therapeutic agent for GBS and or Fisher syndrome administering a test agent to the mouse of claim 3and observing and assessing the degree of symptoms of GBS and or Fisher syndrome. Claim 7 is directed to a therapeutic agent for GBS and or Fisher syndrome by administering a test substance to mouse of claim 3 and measuring and assessing the level of anti GQ1b antibody present in the mouse. Claims 8 and 9 are directed to a therapeutic agent obtained by screening method of therapeutic agent set forth in claims 6 and 7.

Since these claims are broad in scope, encompassing immunizing homozygous mouse that could be used as animal model for GBS or Fisher syndrome. The disclosure provided by the applicant, in view of prior art, must encompass a wide area of

knowledge to a reasonably comprehensive extent. In other word each of those aspect considered broad must be shown to a reasonable extent so that one of the ordinary skill in the art at the time of invention by applicant, would be able to practice the invention without any undue burden being on such Artisan.

The specification broadly describes GBS as inflammatory demylinating disorder of peripheral nerves that is characterized by rapidly progressing flaccid motor paralysis, loss of deep tendon reflexes, dysphagia, articulatory disorder, deep sensory disturbance and vegetative necrosis (see page 1). It is noted that the specification also teaches Fisher syndrome is same as GBS (see page 3, para. 2, of the specification). The specification discloses immunizing FcγRIIB deficient mice with ganaliosides to generate GBS system (see page 5, last para). Page 6-7 describes brief disclosure of the invention and provides brief description of drawing. Page-8-11 broadly describes the best mode of carrying the invention to obtain a mouse model of GBS. Remaining specification describes the specific example of the mouse carrying characteristics similar to one described in this office action. Example 1: of specification teaches immunization of FCγRIIB knockout mice with GQ1b. The FCγRIIB-/- mice immunized with GQ1b show peripheral neuropathy including paralysis of their tail and hind legs (see page 14 of the specification). Example 2 shows that FCγRIIB-/- mice immunized with GQ1b show GBS as compared to wild type control. Example 3 shows that FCγRIIB-/- mice immunized with GQ1b show increased level of IgG1, IgG2a and IgG2b antibody against GQ1b as compared to wild type mice (see page 15 and Figure 3). It is noted that specification describes that FCγRIIB transgenic mouse can be generated by substituting the exon S2 and EC1 with a neo gene cassette (see page 12, paragraph 3 of the specification and also evidenced by Takai, Nature, 1996, 379, 346-349, IDS; see figure 1a).

However, such broad disclosure does not demonstrate the information required by the Artisan to reasonably predict disclosed phenotype in any FcγRIIB deficient mouse. The specification does not provide any specific guidance as to how a heterozygous mouse or any other mouse would show the same peripheral neuropathy

after immunization with GQ1b. In fact, Applicant's examples only describe a homozygous FcγRIIB -/- mouse immunized with GQ1b showing spreading of hind legs, inability of walking and dropping tail (claim 1, page 14, para. 1). At the time of the invention, although many of the methods are routine, neither art of record nor the specification teaches how to practice the claimed invention for heterozygous Fc□RIIB +/- mouse as recited in the claimed invention. Furthermore, the specification does not teach any other genetic disruption involving Fc□RIIB gene. Therefore, it is apparent that any other genetic disruption including substitution or substitution of other exons will not result in same phenotype. It is noted that the specification as filed does not provide any specific information for practicing the claimed mouse model except the Fc□RIIB -/- knockout mouse model and peripheral neuropathy associated with the immunization of instant mouse with GQ1b. An artisan would have to carry out extensive experimentation to make and use the invention in immunizing FcγRIIB -/- knockout mouse or any other mouse with partial deletion in the genome to show that it would also result in peripheral neuropathy. These experiments would have been undue because of the art of making transgenic mice without any specific phenotype to study diseases model were unpredictable and specification fails to provide any guidance as to how the claimed method would have been practiced.

Claims 1-3 encompass GBS mouse model by immunizing an FcγRIIB -/- mouse with GQ1b primarily due to deficiency in FcγRIIB gene. The specification only teaches the phenotype after immunizing FcγRIIB-/- null homozygous mouse. It is emphasized that, Holschneider et al. (Int J Devl Neuroscience, 2000, 18: 615-618, art of record) state that single genes are often essential in a number of different physiological processes. Hence deletion of an individual gene in mouse may prove so drastic or so widespread as to create an amalgam of phenotypes whose interpretation becomes confounded by the interaction of various new physiologic changes (pp 615). Holschneider et al discuss various factors that contribute to the resulting phenotype of transgenic mice, including compensatory system that may be activated to mask the resulting phenotype; these compensatory changes may be due to differential expression

of another gene, which may be regulated by the downstream product of the deleted gene. It is not apparent how skilled artisan without any undue experimentation, practices method as contemplated by the instant claims particularly given the unpredictability of the resulting phenotype of a mouse due to deletion of gene. In fact prior art recognizes that the resultant phenotype, when producing knockdown mice, is exceedingly unpredictable. Griffiths (Microscopy Research and Technique 1998, 41: 344-358, art of record) taught that, despite a known role for the PLP gene based on spontaneous mutations in the gene, the knockout mouse failed to display any of the expected phenotype (pp 350, last paragraph). Therefore, the specification does not enable for any other mouse whose FcγRIIB gene function is deficient other then the transgenic mouse model comprising a homozygous disruption of FCγRIIB that is specifically disclosed in the instant application having the disclosed phenotypes.

Claims 1-2 embrace transgenic mouse deficient in FCγRIIB as a model for GBS or Fisher syndrome without any specific phenotype; subsequently limiting to a mouse that develops peripheral neuropathy consistent with paralysis of its tail and hind legs and also shows elevated levels of antibody against GQ1b. The specification teaches that an inflammatory demyelinating disorder of peripheral nerves which occurs a few weeks after a flu-like symptom, and is characterized by rapidly-progressing flaccid-motor paralysis (weakness in muscles of all four limbs), loss of deep tendon reflexes, dysphagia, articulatory disorder, deep sensory disturbance, and vegetative neurosis (cardiac arrhythmia, blood pressure fluctuation) (see page 1, paragraph 2). In addition, specification also broadly discloses that Fisher syndrome is known as a variant of GBS. It is noted that specification describes the symptoms of Fisher syndrome that includes external ophthalmoplegia, diplopia, ataxia, loss of tendon reflexes, and facial nerve palsy, with a preceding infection of the upper respiratory tract. It is noted that immunization of mice with GQ1b shows peripheral neuropathy and paralysis of tail and hind legs but fails to provide any evidence that these mouse show characteristic consistent with other symptoms of GBS or Fisher syndrome such as weakness in forelimb, dysphagia, articulatory disorder, deep sensory disturbance, and vegetative

neurosis (cardiac arrhythmia, blood pressure fluctuation. It is emphasize that syndrome is defined as the aggregate of symptoms and signs associated with any morbid process, and constituting together the picture of the disease (See Stedman's Medical Dictionary 27th Edition). In the instant case, the specification only teaches mouse immunized with GQ1b show paralysis or tail and hind limbs without showing any other symptoms or any histopathology of any demylination consistent with GBS or Fisher syndrome. Prior to instant invention, art teaches that even intra dermal inoculation of mouse with HSV-1 shows symptoms such as hind-limb paralysis, flaccid tail and loss of bladder control within 6-7 days post infection (see abstract, Reinhard et al Adv Exp Med Biol. 1996; 398:241-6, art of record). Kennel et al (Neurobiol Dis. 1996; 3(2):137-47, art of record) also teach a mouse autosomal recessive mutation progressive motor neuronopathy (pmn) that results in early onset motor neuron disease with rapidly progressive hindlimb paralysis, severe muscular wasting, and death at around 6 weeks of age (see page 141, col. 2). These studies suggest that hind limb or tail paralysis cannot be solely rely as phenotype for GBS or any specific syndrome. Claims 6-9 are directed to a therapeutic agent and method of identifying test agent for GBS and or Fisher syndrome. The disclosure provided guidance in terms of elevated level of antibody titer of GQ1b after immunizing the transgenic mouse of the invention, however it does not provide any guidance in terms of its functional involvement in GBS or FS nor does it disclose a relationship to a condition associated with these syndromes that could be treated by any agent identified by the instant methods. Therefore, because an artisan does not know the function any known relationship to a disease or condition, and artisan would not know how to use any identified compounds. As amended claim 3 also require mouse model of GBS wherein mouse shows elevated level of GQ1b antibody. It is noted that Chaudhry et al (Seminar Opthalmol 2006 Oct-Dec;21(4):223-7) report "association of the GQ1b IgG antibody and several GBS variants, particularly the Fisher syndrome and those associated with ophthalmoparesis. We present three cases of GBS variants. All three cases had associated ophthalmoplegia but only one of the three had a positive GQ1b antibody association". Odaka et al (J Neurol Neurosurg Psychiatry. 2001 Jan;70(1):50-5.) report that "term "anti-GQ1b IgG antibody syndrome"

is not intended to be used as a clinical diagnosis, but recognition of this syndrome is useful for understanding the aetiological relation among the various illnesses and for introducing the established treatments of GBS for use with other conditions (see abstract). Thus, it is apparent that elevated level of GQ1b antibody does not provide adequate guidance in developing GBS or FS as broadly embraced by claims 1-3 and 6-9). An artisan would have to perform undue experimentation to determine other symptoms in the instantly claimed mouse model to determine whether this could in fact be a model for any syndrome. Furthermore, for an artisan to use or make the instant method for its intended use, an artisan would have to determine the function of phenotype of mouse model set forth in claims 1-3 and then establish the nexus between level of antibody titer and the specific peripheral neuropathy seen in the mouse to any disease or specific conditions as broadly classified as GBS or FS. Therefore, given the act that an artisan would not know how to make or use the instant method for identifying an agent that modulates broadly recited symptoms. It is emphasized that the specification does not provide any specific guidance for the use of a method for identifying agents that treat GBS or Fisher syndrome. It is noted that specification does not provide any guidance in terms of flu-like symptom or deep sensory disturbance or cardiac arrhythmia, blood pressure fluctuation as broadly associated with GBS (see page 1, paragraph 2) or any infection of the upper respiratory tract. Furthermore, there is no specific teaching regarding how individual symptoms are related specifically to any condition or type of agents, amount needed, dosage schedule and delivery route that would be used to identify the agent. An artisan would have to perform undue experimentation to first establish a link between the immunizing transgenic animal of the invention with GQ1b with a specific syndrome and then test various parameters using different type of agents, dosage and delivery route in order to reduce symptoms seen the transgenic animal of the invention. It is emphasized that neuropathy symptoms in a disease or condition could be caused by a variety of mechanism and that may or may not have any involvement of GQ1b immunization. Given that the specification and art do not provide any specific guidance and therefore, an artisan would not know if the instant mice represent a model for GBS or FS that could be used to screen therapeutic

agent for the treatment of GBS or FS. In addition, specification has only exemplified a method to compare the elevated antibody of GQ1b in wild type and transgenic mouse of the invention. An artisan would not know if a particular agent identified using the mouse disclosed in the invention would be able to treat a disease symptom similar to those observed in the knockout mouse. An artisan would have to do further experimentation to determine if the symptoms associated with the knockout are associated with the disease and therefore representative a GBS or FS. In view of foregoing discussion, it is apparent that any difference of symptom seen in the instant transgenic mouse cannot be generally associated with any complex disorder such as GBS or FS. Therefore, an artisan would not know if the compounds identified by measuring few parameters in the transgenic mouse of the invention would be effective for its intended use in the treatment of GBS or FS as contemplated in the instant application.

In conclusion, in view of breadth of the claims and absence of a strong showing by the Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by the Applicant is not enabled for the claimed inventions commensurate in scope with these claims. The specification and prior art do not teach a mouse model that would be GBS or Fisher mouse model. An artisan of skill would have required undue experimentation to practice the method as claimed as supported by the observations in the art record.

Response to Arguments

Applicant's arguments filed March 5, 2007 have been fully considered but they are not fully persuasive. Applicants argues that MPEP §2164.01 states that a specification only needs to provide "sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention." Therefore, applicants do not need to demonstrate every gene knock out method. Applicants further assert that technology is well-known in the art, therefore one of ordinary skill in the art would be able to make and use the invention from the

description in the instant specification and with what is commonly known in the art (see page 9 of the arguments).

In response, it is noted that independent claims 1 and 2 recite a GBS and FS mouse model that is obtained by immunizing homozygous Fc gamma RIIB gene deficient mouse with GQ1b ganglioside. These claims do not recite any specific phenotype for the resulting mouse model. Prior art teaches that resulting phenotype of a mouse is unpredictable. Holschneider et al. (Int J Devl Neuroscience, 2000, 18: 615-618) state that single genes are often essential in a number of different physiological processes. Hence, deletion of an individual gene in mouse may prove so drastic or so widespread as to create an amalgam of phenotypes whose interpretation becomes confounded by the interaction of various new physiologic changes (pp 615). Similarly, Griffiths (Microscopy Research and Technique 1998, 41: 344-358) taught that, despite a known role for the PLP gene based on spontaneous mutations in the gene, the knockout mouse failed to display any of the expected phenotype (pp 350, last paragraph). Therefore, there is no evidence on record that any other gene disruptions, including substitution of other domains or exons as argued by the applicants will not necessarily cause the same change in activity of the FcγRIIB gene product as the disruption exemplified in the specification. Given such differences in the gene disruption of transgene, particularly when taken with the lack of guidance in the specification for any transgenic mouse with any specific phenotype, it would have required undue experimentation to establish the levels of the transgene product, the consequences of that product, and therefore, the resulting phenotype. It is difficult to predict what activity level and what phenotype a resulting mouse would have with any other gene disruption.

With respect to applicants argument that instant application describes, the Fcamma RIIB gene deficient mouse immunized with GQ 1 b ganglioside showing a distinct phenotypic response compared to a wild-type mouse, namely paralysis of the tail and hind legs and elevated level of antibody titer against GQIb(see figure 1-3 of the specification). It is noted that the features upon which applicant relies (i.e., antibody titer and other specific phenotype) are not recited in the rejected claims 1-2. Although the claims are interpreted in light of the specification, limitations from the specification are

not read into the claims. It is noted that the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991)*. It is also well established in case law that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994)*, citing *In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991)*. An artisan would have to perform undue experimentation to immunize homozygous Fc gamma RIIB gene deficient mouse and then establish said mouse as model for GBS and FS as broadly recited in claims 1-2.

Withdrawn-Claim Rejections - 35 USC § 112

Claims 1-3 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments to claims 1 and 3. Since remaining claims were not treated on merit, and instant rejection was limited to only to claims 1-3 as stated before.

New- Claim Rejections-Necessitated by amendments - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites a limitation "according to" that simply requires bringing into agreement. Since, according to only implies a level of agreement between two, thus metes and bound of instant claim 2 is unclear and this limitation does not further limit

the instant claim. It is emphasized that specific reference to the mouse will obviate this rejection. Appropriate correction is required.

Claims 6-9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Instant claims uses a transgenic mouse for treating screening therapeutic agents, but the does not set forth any steps involved in method/process, it is unclear what method /process applicant is intending to encompass. The claim merely recites a method of immunizing homozygous FcγRIIB-/- mouse and then observing the degree of symptoms of GBS and or FBS that includes measuring levels for antibody against GQ1b without any active, positive step delineating how up, down or same level of antibody would actually mean to the method of screening. Further, method steps do not positively link to the preamble of the method claims. Claims 8 and 9 are directly or indirectly depend on claim 6. Appropriate correction is required.

Withdrawn-Claim Rejections - 35 USC § 102

Claims 2-3 rejected under 35 U.S.C. 102(b) as being anticipated by Reinhard et al Adv Exp Med Biol. 1996; 398:241-6 is withdrawn in view of amendments to the claims.

Withdrawn-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 rejected under 35 U.S.C. 103(a) as being unpatentable over Takai et al (Nature, 1996, 379, 346-348, IDS), Yuki (Ann Neurol, 2001, 49, 712-720) and Odaka et al (J Neurol Neurosurg Psychiatry. 2001; 70(1): 50-5) is withdrawn. Applicants argument is persuasive to the extent that cited reference of Yuki et al do not provide motivation to immunize mice with GQ1b with reasonable expectation of success as Yuki et al failed to induce IgG against GQ1b (see table 2 and 3).

Conclusion

No Claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Takai et al (Nature, 1996, 379, 346-348, IDS),

Yuki (Ann Neurol, 2001, 49, 712-720, IDS)

Odaka et al (J Neurol Neurosurg Psychiatry. 2001; 70(1): 50-5, IDS)

Bowes et al (Infection and Immunity, 2002, 70(9), 5008-5018).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anoop Singh
AU 1632

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER